REMARKS

With this amendment, claims 13-21, 31, 43, 46, 53, 66-71, 74, and 76-79, and 83 are pending. Claims 14 and 66 are canceled. Claims 1-12, 22-30, 32-42, 44, 45, 47-52, 54-65, 72, 73, 75, and 80-88 are withdrawn.

With this amendment, claims 13, 15, 16, 31, 68, 69, and 74 have been amended. Support for the amendment to claim 13 may be found in the application as filed, for example, original claim 58, 68, and 76. Support for the amendment to claim 15 may be found in the application as filed, for example, at page 4, paragraph [0015]. Support for the amendment to claim 16 may be found in the application as filed, for example at pages 12-13, paragraph [0055]. Support for the amendment to claims 31 and 74 can be found in the application as filed, for example, at pages 12-13, paragraph [0055], page 23, paragraph [0085], page 24, paragraph [0086], and pages 24-25, paragraph [0088]. Support for the amendment to claim 68 may be found in the application as filed, for example, at page 3, paragraph [0012] and in original claim 66. Support for the amendment to claim 69 can be found in the application as filed, for example, at page 52, paragraph [0159].

I. Objection to the Specification

The Office has objected to the specification, stating that the specification contains an embedded hyperlink or other browser executable code in paragraph [0070] on page 17 of the application as filed.

Applicant has amended paragraph [0070] to remove the embedded hyperlink by deleting the text "http://". Accordingly, the Office's objection to the specification is rendered moot.

II. Objections to the Claims

A. Claim 16

The Office objects to claim 16 as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claim 16 has been amended to depend from claim 13. As such, claim 16 further limits the subject matter of the claim from which it depends. Accordingly, the Office's objection to claim 16 is rendered moot.

B. Claim 14

The Office objects to claim 14 as being in improper form, stating that multiple dependent claims must be stated in the alternative.

With this amendment, claim 14 has been canceled. Accordingly, the Office's objection to claim 14 is rendered moot.

Claim 20

The Office objects to claim 20 for stating "any one of" while being dependent upon only one claim.

Claim 20 has been amended to remove the phrase "any one of." Accordingly, the Office's objection to claim 20 is rendered moot.

III. 35 U.S.C. § 112, Indefiniteness

Reconsideration is requested of the rejection of claims 13, 14, 16-19, 31, 43, 46, 53, 66, 67, 69, and 74 under 35 U.S.C. 112, second paragraph for indefiniteness.

A. Claims 13, 14, 66, 67, and 69

The Office asserts that claims 13, 14, 66, 67, and 69 are indefinite in the recitation of "OBP" or "OBP3", stating that such designations are arbitrary and create ambiguity in the claims. Applicant respectfully disagrees.

With this amendment, claims 14 and 66 have been canceled. Accordingly, the rejection as applied thereto is rendered moot.

As noted in the specification, OBP is an abbreviation for an OBF (ocs binding factor) binding protein.[1] An OBP is a member of the Dof (domain of one finger) family of transcription factors, this family of transcription factors sharing a conserved DNA-binding domain comprising 52 amino acid residues in which a $CX_2CX_{21}CX_2C$ motif is predicted to form a single zinc finger.[2] A particular OBP is the OBP3 of *Arabidopsis thaliana*,[3] a particular embodiment of which is represented by the nucleotide sequence of SEQ ID NO: 1 and the polypeptide sequence of SEQ ID NO: 2.[4]

Moreover, the use of the designations OBP, OBP1, OBP2, OBP3, etc is well known in the art. Particularly, references published before the priority date of the present application,[5] around the filing date of the present application,[6] and after the filing date of the present application[7] consistently use the designations OBP, OBP1, OBP2, OBP3, etc. As such, use of the designations "OBP" and "OBP3" is not arbitrary and does not create ambiguity in the claims.

The above notwithstanding, claims 13, 67, and 69 have been amended such that the reference to "OBP" or "OBP3" is defined by specific reference to SEQ ID NO: 1 or variants thereof, thereby further making clear what is defined by the terms "OBP" and "OBP3."

Accordingly, Applicant respectfully requests withdrawal of the objection to claims 13, 14, 66, 67, and 69.

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[1] Application as filed, page 2, paragraph [008] and page 15, paragraph [0067].
[2] Application as filed, page 2, paragraph [008] and page 15, paragraph [0067].
[3] Application as filed, page 2-3, paragraph [0009] page 3, paragraph [0012], and page 4, paragraph [0013].
[4] Application as filed, page 4, paragraph [0015].
[5] *See*, for example, Kang, H.G. & Singh, K.B., Plant Journal, 21(4): 329-339 (2000) (cited as reference number 61 in Applicant's Information Disclosure Statement mailed April 20, 2006).
[6] *See*, for example, Hong-Gu, K. et al., Plant Journal, 35(3): 362-372 (2003) (copy enclosed).
[7] *See*, for example, Ward, J.M. et al., Plant Cell, 17(2): 475-485 (2005) (copy enclosed).

B. Claim 66

The Office asserts that Claim 66 is indefinite in its recitation of "wherein said antisense nucleic acid sequence results in an increase," stating that it is not clear how an antisense nucleic acid sequence can result in anything.

Claim 66 has been canceled, thereby rendering the Office's rejection of the same moot. The language of claim 66 has, however, been inserted into amended claim 67. This language has been amended such that it now recites that expression of said antisense nucleic acid sequence in the plant cell results in an increase in the size of a resulting plant as compared to a corresponding wild-type variety of plant. Such an amendment eliminates the language objected to by the Office, thereby rendering the Office's objection to the same moot.

C. Claim 69

The Office asserts that claim 69, which depends from claim 66, lacks antecedent basis for the phrases "or plant part" and "the nucleotide sequence in (b)."

Claim 69 has been amended to add the term "cell" and to delete the phrase "or plant part." The claim has also been amended to change the claim dependency from claim 66 to claim 68, thereby providing antecedent basis for the phrase "the nucleotide sequence in (b)." Accordingly, the Office's indefiniteness objection to claim 69 has been rendered moot.

D. Claims 16, 31, and 74

The Office asserts that the recitation of the phrase "stringent conditions" is indefinite, stating that Applicant does not explicitly disclose specific hybridization conditions that define Applicant's recitation "stringent conditions."

Claims 16, 31, and 74 have been amended to reflect that the stringent conditions are a wash stringency equivalent to 0.2X SSC, 0.1% SDS at 50°C. Such an amendment specifically defines the stringent conditions, thereby obviating the Office's rejection.

IV. 35 U.S.C. § 112, Written Description

Reconsideration is requested of the rejection of claims 13, 14, 16-21, 31, 43, 46, 53, 66-71, 74, and 76-79 under 35 U.S.C. 112, first paragraph for lack of written description.

With this amendment, claims 14 and 66 have been cancelled. Accordingly, the rejection as applied thereto is rendered moot.

The Office rejected the aforementioned claims as unpatentable because Applicant did not "identify essential regions of the OBP3 protein encoded by SEQ ID NO: 1," nor does Applicant "describe any polynucleotide sequences that hybridize to SEQ ID NO: 1 under stringent conditions or wash conditions as specified for example in claim 68 and which encodes a polypeptide having activity differing from that of Arabidopsis thaliana OBP3 by about 10%, 20%, 30%, or 40%." In support of the rejection under the written description requirement, the Office action cites *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 U.S.P.Q. 2d 1398 (Fed. Cir. 1997). Applicants respectfully traverse.

Applicant is claiming transgenic plant cells comprising an antisense nucleic acid sequence described according to a specific sense sequence, the expression of the antisense sequence which results in the increase of the size of the pant in which it is expressed; seeds produced from plants comprising the transgenic plant cell; recombinant antisense expression vectors comprising antisense nucleotide sequences that are capable of hybridizing to mRNA encoding an Arabidopsis thaliana OBP3, wherein the Arabidopsis thaliana OBP3 is described according to a specific nucleic acid sequence; methods of producing transgenic plants having increased size compared to wild-type plants utilizing the recombinant expression vectors; methods of altering the size of the aerial portion of a plant without dwarfing the root tissues utilizing the recombinant antisense expression vectors; and transgenic plant cells comprising an antisense nucleic acid sequences complementary to nucleic acid sequences encoding an OBP3 polypeptide, wherein the OBP3 polypeptide is described according to a

specific sequence, and the expression of the antisense sequence results in the increase of the size of the pant in which it is expressed.

Notably, Applicant has defined the OBP in these claims according to a particular sequence -- namely SEQ ID NO: 1 and sequences that hybridize under specific stringency conditions. In addition, Applicant has also required that the OBP in the claimed subject matter also have a requisite activity - namely, the ability to affect plant stature as described in the specification. Because of the relationship between antisense and related sense sequences, the OBP antisense sequence is necessarily defined by SEQ ID NO: 1 - namely, being complimentary to SEQ ID NO: 1. Likewise, the function of the antisense sequence is also defined by the function of the OBP sense sequence - namely, the antisense sequence has the ability to limit or prevent the function or expression of the sense sequence.

Moreover, consistent with the rule opined in *Eli Lilly*, Applicant has identified a representative number of sequences encoding a polypeptide that affects OPB expression. In addition to SEQ ID NO: 1, Applicant identified SEQ ID NOS: 12, 13, 14, 15, 16, 17, 18, 19, and 20, each of which is a nucleic acid sequence encoding a polypeptide that affects OBP expression. Naturally, therefore, Applicant has also identified a comparable number of antisense coding nucleic acids -- namely, nucleic acid sequences that are antisense to each of SEQ ID NOS: 12, 13, 14, 15, 16, 17, 18, 19, and 20.

In contrast to *Eli Lilly*, therefore, Applicants are claiming transformed plant cells, seeds, recombinant expression vectors, and methods of affecting plant stature, each of which comprises or utilizes nucleic acid sequences described with reference to specific nucleic acid sequences having defined structural and functional characteristics. Moreover, Applicant has recited a representative number of these sequences. As such, Applicant has provided adequate written description to support claims 13, 16-21, 31, 43, 46, 53, 67-71, 74, and 76-79.

V. 35 U.S.C. § 112, Enablement

Reconsideration is requested of the rejection of claims 13-21, 31, 43, 46, 53, 66-71, 74, and 76-79 under 35 U.S.C. 112, first paragraph as being unpatentable for lack of enablement.

With this amendment, claims 14 and 66 have been cancelled. Accordingly, the rejection as applied thereto is rendered moot.

The Office first asserts that Applicant has not explicitly defined SEQ ID NO: 1, disclosing that while cloning the gene responsible for the mutant phenotype, extra 3' and 5' DNA was included and that Applicant is silent as to the start and stop codons for the corresponding encoded protein. The Office contends therefore, that using DNA that hybridizes to the extra 5' and 3' regions will not silence an endogenous gene using antisense technology because the 5' and 3' regions are not transcribed. Likewise, the Office asserts that DNA that hybridizes to bases 6179-7538 of SEQ ID NO: 1 (comprising the 35S promoter) will also not result in the down regulation of an endogenous gene when used in antisense technology.[8]

Applicant notes that the rejected claims require more than the simply use of an antisense nucleic acid sequence having certain structural characteristics (e.g. being complementary to SEQ ID NO: 1 or hybridizing to SEQ ID NO: 1 and being of a certain length). Each of the rejected claims also requires that expression of the antisense nucleic acid sequence have the particular effect of increasing the size of the plant containing the antisense nucleic acid sequence. Therefore, even if a sequence were to hybridize to only the extra 3' or 5' regions or the 35S promoter region of SEQ ID NO: 1 and use of this sequence as an antisense sequence did not silence or down regulate the endogenous gene, the sequence would fall outside the scope of the claims, as the claims require ***both*** a particular structure ***and*** a particular function. As an applicant is not required to enable embodiments that fall ***outside the scope of the claims***, the particular examples provided by the Office have no bearing on the enablement of Applicant's claims.

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[8] Office action mailed March 24, 2006, page 10.

The Office asserts that Applicant discloses that he intentionally excluded the nucleic acid segment encoding the Dof domain in his construct. The Office contends, therefore, that using DNA that hybridizes to this region in antisense technology would produce unexpected results, as other genes that are not responsible for the Applicant's claimed phenotype would be down regulated. By way of example, the Office cites to Papi et al.[9] which is asserted to teach that the DAG1 protein, comprising a Dof domain, is involved in light responses and integrity of the tests of Arabidopsis. The Office contends, therefore, that using the Dof domain in an antisense construct will down regulate genes not involved in plant stature and will not increase the size of the plant.

As noted by the Office, Applicant did intentionally exclude the nucleic acid encoding the Dof domain from the construct used. This was done in order to prevent the very effect the Office contends could occur by using DNA that hybridizes to the Dof domain - namely, the down regulation of genes that affect phenotypes other than those affecting plant structure. Accordingly, application of Papi et al., which discloses the affects of a protein ***containing a Dof domain***, is not indicative of the claimed invention, which does not contain the Dof domain; therefore, this reference has no bearing on the enablement of the same.

Moreover, the claims of the present application require that the sequence cited therein meet certain structural and functional requirements. The isolation and use of antisense nucleic acid sequences that fail to meet each of these requirements falls outside the scope of the claims, and therefore, need not be enabled. Accordingly, a sequence meeting the structural requirements, but not the functional requirements of the claims, as that disclosed in Papi et al., does not fall within the scope of the claims. As an applicant is not required to enable embodiments that fall ***outside the scope of the claims***, the particular example provided by the Office has no bearing on the enablement of Applicant's claims.

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[9] Papi et al., Plant Physiology, 128: 411-417 (2002).

The Office further asserts that "[a]ntisense constructs can behave unpredictably when transformed into a heterologous plant species."[10] In support of this proposition, the Office cites Colliver et al.,[11] which discloses that the transformation of bird's foot trefoil (*L. corniculatus*) with a construct that is antisense to bean (*P. vulgaris*) chalcone synthase resulted in at least some transformed plants that had increased levels of chalcone synthase which is contrary to the expected result. However, as noted in the Colliver et al., CHS is encoded by a **complex gene family** in bird's foot trefoil of four to eight genes with differential genome organization in the various transformed lines. Notably, Colliver et al. disclose that "CHS is encoded by a heterologous gene family in *L. corniculatus* [bird's foot trefoil] and that such data [obtained in their study] indicate that *L. corniculatus* CHS genes **with higher homologies** to CHS17 [from *P. vulgaris*] may be **more susceptible to antisense suppression** than lower homology CHS genes."[12] As Applicant's claims require a certain percent homology between an antisense sequence complementary to SEQ ID NO: 1 and an antisense sequence that would hybridize to the same, Colliver et al. cannot be said to be indicative of the enablement of Applicant's claimed invention. In fact, the quoted passage from Colliver et al. would appear to support Applicant's assertion that claims encompassing antisense constructs containing antisense sequences from one plant species used to down regulate expression of a related sense sequence in another plant species are enabled if the antisense sequence from the one plant species shares at least a certain percent homology to the related antisense or sense sequences of the different plant species in which the antisense sequence is to be inserted.

Moreover, numerous examples of the transformation of one species of plant with an antisense construct containing an antisense sequence from a different species of plant that resulted in the expected suppression/inhibition of transcription of the sense strand have been reported. For example, Faske et al.[13] report the **stable reduction** of NADP-MDH in tobacco plants transformed with a construct containing the expression of

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[10] Office action mailed March 24, 2006, page 11.
[11] Colliver et al., Plant Molecular Biology 35: 509-522 (1997).
[12] Colliver et al., page 519, left column (emphasis added).
[13] Faske et al., Plant Physiology, 115(2): 705-715 (1997) (copy enclosed).

the heterologous pea *Nmdh* cDNA in an antisense orientation.[14] In fact, in the sole instance where the antisense construct resulted in elevated NADP-MDH expression, Faske et al. noted that this result was "obscure" and therefore "not analyzed further."[15] Moreover, Faske et al. note that "it has been shown previously that silencing of endogenous genes can be similarly achieved by transformation with closely related but nonidentical sequences (e.g. Phe ammonia lyase from bean in transgenic tobacco plants [Elkind et al., 1990]; and, recently, NADP-MDH from *S. bicolor* in transgenic tobacco plants [Trevanion et. a [sic]., 1997])."[16] This clearly demonstrates that antisense constructs containing antisense sequences from one plant species may be used with success to down regulate expression of a related sense sequence in another plant species and that those of skill in the art were both aware and capable of performing such transformations well before (approximately five years) the priority date of the present application.

The Office also cites Emery et al.[17] noting that this reference discloses experiments in which a target sequence of a micro-RNA that was changed by two base pairs caused the complementary micro-RNA not to bind to the target sequence, which subsequently led to an increased expression of the target sequence's encoded protein. Applicant notes that Emery et al. is contrary to the disclosure of Faske et al. discussed above, wherein the endogenous target sequence of the pea antisense sequence used therein differed from the target sequence in the tobacco plant in which the pea antisense construct was successfully used to stably reduce NADP-MDH expression in tobacco plants.

The Office further asserts that the state of the art is such that one of skill in the art cannot predict which nucleic acids that hybridize to SEQ ID NO: 1 and comprise at least 15 contiguous nucleotides will encode a protein with the same activity as a protein encoded by SEQ ID NO: 1.

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[14] Faske et al., page 709, left column.
[15] Faske et al., page 709, left column.
[16] Faske et al., page 709, left column.
[17] Emery et al., Current Biology, 13: 1768-1774 (2003).

Applicant notes that claims 31 and 74 which recited the requirement that the OBP nucleic acids which hybridize to SEQ ID NO: 1 comprise a nucleotide sequence of at least 15 contiguous nucleotides have been amended to remove this language. In place thereof is the requirement that the nucleic acids have at least 70% homology to SEQ ID NO: 1 or a sequence complementary to SEQ ID NO: 1, and nucleotides encoding conservative amino acids substitutions.

The Office also cites Bowie et al.[18] in support of its assertions that the "prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited."[19] However, Bowie et al. disclose that "many different sequences can code for proteins with essentially the same structure and activity,"[20] and that "[s]tudies in which these methods [for studying protein tolerance to sequence variation] were used have revealed that proteins are surprisingly tolerant of amino acids substitutions."[21]

While perhaps complex, such a determination is not undue, but instead is rather routine today as opposed to 1990 when Bowie et al. was published. Furthermore, "the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed," *In re Wands*, 858 F.2d at 737, a significant factor in demonstrating that experimentation is not undue. Specifically, as noted above, claims 31 and 74 have the added requirement that the nucleotides encode conservative amino acids substitutions. The specification describes such substitutions in a protein sequence which would be expected to have minimal to no impact on protein structure or function and can be readily devised by a person of ordinary skill in the biochemical arts.[22] That is to say, it is well known in the art, and was at the time of the filing of this application, that certain amino acids in a peptide or protein can be

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[18] Bowie et al., Science, 247: 1306-1310 (1990).
[19] Office action mailed March 24, 2006, page 11.
[20] Bowie et al., page 1306, left column.
[21] Bowie et al., page 1306, right column.
[22] Specification as filed, pages. 23-24, paragraphs [0085] and [0086].

substituted for other amino acids having a similar hydropathic or hydrophilic index or score, charge, size, etc, and still produce a resultant peptide or protein having similar biological activity. *See* Kyte and Doolittle (J. Mol. Biol., 157: 105-132, 1982) (discussing hydropathic indices); U.S. Patent No. 4,554,101 (discussing hydrophilic indices); and U.S. Patent No. 5,646,008 (discussing substitution of amino acids within a protein with amino acids having similar side chains using site directed mutagenesis techniques).

The Office also cites McConnell et al.[23] for the proposition that proteins may be sensitive to substitutions in even a single amino acid in a protein. However, the goal of McConnell et al. was not to seek out conservative substitutions that retain the activity of the altered protein, but instead substitutions that would disrupt the regulation of certain domains of a protein.

Specifically, McConnell et al. were attempting to determine genes in *Arabidopsis* ***that would alter*** the perception of radial positional information in the leaf primordium and thereby transform abaxial leaf fates into adaxial leaf fates.[24] In so doing, McConnell et al. altered a number of *phb* alleles in the START domain, two of which contained a guanine to adenine change (*phb-1d* and *phb-2d*) and the remaining of which contained a glycine to glutamic acid change (*phb-3d*, *phb-4d*, and *phb-5d*). In so doing, McConnell et al. note that "[i]f the predicted START domain in these family members has a regulatory function, ***we expect to find mutations that disrupt*** this regulation."[25]

In addition, the amino acid substitutions made by McConnell et al. were not conservative substitutions as described in Applicant's specification and required by Applicant's claims. Particularly, from the copy of McConnell et al. provided by the Office, it is impossible to determine the resultant amino acid substitution from the guanine to adenine substitution in *phb-1d* and *phb-2d*. However, assuming this substitution to be the glycine to alanine substitution cited by the Office,[26] this substitution would be expected to affect a change in function, as this is a ***non-conservative*** substitution of a neutral polar amino acid (glycine) with a neutral nonpolar

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[23] McConnell et al., Nature, 411: 709-713 (2001).
[24] McConnell et al., page 709, Abstract.
[25] McConnell et al., page 710, left column (emphasis added).
[26] Office action mailed March 24, 2006, page 11.

(hydrophobic) amino acid (alanine). Likewise, the substitution of a glycine residue for a glutamic acid residue would also be expected to affect a change in function, as this is a ***non-conservative*** substitution of a neutral polar amino acid (glycine) with an acidic (negatively charged) amino acid. Accordingly, McConnell et al. is not indicative of the enablement of Applicant's invention, as the substitutions disclosed therein are not conservative substitutions as required by Applicant's claims.

Finally, the Office asserts that Applicant has not disclosed how to make or isolate any of the sequences encompassed by the broad claims, asserting that Applicant has not taught which regions of the respective polynucleotides can be used to amplify any of the polynucleotides or which regions may be used to isolate any of the polynucleotide sequences. Therefore, undue trial and error experimentation would be required for one of skill in the art to screen through non-exemplified sequences.

Applicant notes that enablement does not preclude any testing or experimentation, just ***undue*** testing or experimentation. It is well settled that the test for undue experimentation is "not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Simple experimentation to determine whether antisense sequences would have the required structural and functional characteristics would fall within the realm of routine experimentation and would not render the claims nonenabled.

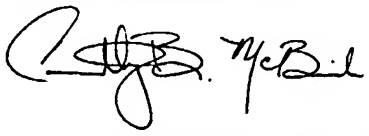
As such, Applicant has adequately enabled claims 13-21, 31, 43, 46, 53, 66-71, 74, and 76-79.

CONCLUSION

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the objection to the specification and claims 14, 16, and 20; of the rejection of claims 13, 14, 16-19, 31, 43, 46, 53, 66-67, 69, and 74 under 35 U.S.C. 112, second paragraph, for indefiniteness; of the rejection of claims 13, 14, 16-21, 31, 43, 46, 53, 66-71, 74, and 76-79 under 35 U.S.C. 112, first paragraph for lack of written description; and of the rejection of claims 13-21, 31, 43, 46, 53, 66-71, 74, and 76-79 under 35 U.S.C. 112, first paragraph, for lack of enablement.

Applicant requests an extension of time to and including September 24, 2006, 2006, for filing a response to the above-mentioned Office action. The Commissioner is hereby authorized to charge this fee to Deposit Account No. 19-1345.

Respectfully submitted,



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* Enclosures